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LEYDIG VOIT & MAYER, LTD
TWO PRUDENTIAL PLAZA, SUITE 4900
180 NORTH STETSON AVENUE
CHICAGO, IL 60601-6731

EXAMINER	
BARNHART, LORA ELIZABETH	
ART UNIT	**PAPER NUMBER**
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/523,858	BISHOP ET AL.	
	Examiner	Art Unit	
	Lora E. Barnhart	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,12-16,18,19 and 21* is/are pending in the application.

4a) Of the above claim(s) *7,12-16,18,19 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/7/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-7,12-16,18,19 and 21 are currently pending.

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-6, in the reply filed on 8/24/07 is acknowledged. The traversal is on the ground(s) that the claims in Groups I and VI are unified by a special technical feature, *i.e.*, a method for differentiating a stem cell into a cell that expresses surfactant protein C ("SPC"; Reply, page 2, paragraph 4). Applicants further allege that the claims could all be examined without imposing an undue burden on the examiner. These arguments have been fully considered, but they are not persuasive.

37 C.F.R. 1.475 requires that if multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application and the first recited invention of each of the other categories related thereto will be considered as the main invention in the claims. Since the method recited in Group I has different steps from the steps required to practice the method of Group VI as claimed, these two Groups are considered to be two different methods for making SPC-positive cells. In accordance with 37 C.F.R. 1.475, Group I is considered the main invention and Group VI is a separate method.

Applicant alleges that there would be no burden on the examiner in examining all of the claims at once, relying on M.P.E.P. §802.02. Chapter 800, however, is limited to a discussion of the subject of restriction and double patenting under Title 35 of the United States Code and Title 37 of the Code of Federal Regulations as it relates to national

applications filed under 35 U.S.C. 111(a). The discussion of unity of invention under the Patent Cooperation Treaty Articles and Rules as it is applied as an International Searching Authority, International Preliminary Examining Authority, and in applications entering the National Stage under 35 U.S.C. 371 as a Designated or Elected Office in the U.S. Patent and Trademark Office is covered in M.P.E.P. §1850 and is dictated by PCT Rules 13.1 and 13.2. See M.P.E.P. §801. Burden is not a consideration in a finding of lack of inventive unity; rather, according to M.P.E.P. §1850, the only consideration is whether the inventions share a special technical feature.

The requirement is still deemed proper and is therefore made FINAL.

Claims 7, 12-16, 18, 19, and 21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 8/24/07. Examination on the merits will commence at this time on claims 1-6 ONLY.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Specification

The disclosure is objected to because of the following informalities: It does not conform with the requirements of 37 C.F.R. 1.77(b), which describes the sections that should be included in a patent application specification. Appropriate correction is required.

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
(e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
(f) BACKGROUND OF THE INVENTION.
    (1) Field of the Invention.
    (2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(g) BRIEF SUMMARY OF THE INVENTION.
(h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(i) DETAILED DESCRIPTION OF THE INVENTION.
(j) CLAIM OR CLAIMS (commencing on a separate sheet).
(k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of differentiating embryonic stem (ES) cells into cells that express surfactant protein C (SPC) by culturing the ES cells such that they form embryoid bodies and then culturing these embryoid bodies in a particular medium comprising particular amounts of particular growth factors, does not reasonably provide enablement for differentiating any stem cell into SPC-expressing cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands*, 858 F.2d 731, 737, 8 USPQd 1400, 1404 (Fed. Cir. 1988) (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the level of one of ordinary skill; (e) the level of predictability in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. While all of these factors are considered, a sufficient number are discussed below so as to create a *prima facie* case.

The claims, as interpreted for this Office action, are broadly drawn to a method in which any stem cell is cultured under conditions that promote the formation of embryoid bodies and in which embryoid bodies are cultured under conditions that promote their

differentiation to SPC-expressing cells. As discussed below in the rejections under 35 U.S.C. § 112, second paragraph, the method as claimed does not particularly require that step (a) be carried out before step (b). The claim does not describe either the conditions for the formation of embryoid bodies or the conditions for the differentiation to SPC-expressing cells. This breadth is not supported by the teachings of the specification in view of the art.

The cited claims do not place any limit on the type of stem cell to be employed in the method. Even after the time of the invention, however, differentiating a given stem cell type into lung cell types is not considered routine experimentation although the level of ordinary skill is postdoctoral. For example, van Haaften et al. (2006, *Pediatrics Research* 59 Supplement: 94R-99R; reference U) teach that while some reports indicate that mesenchymal stem cells (MSCs) can engraft into lung tissue and differentiate into lung cells (page 96R), other results show that implanted MSCs do not adopt the type II alveolar epithelial cell phenotype (page 97R). Van Haaften concludes that stem cell therapy for lung diseases is at the conceptual stage and is a continuing problem in the art of these diseases (page 98R).

M.P.E.P. § 2164.03 reads, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The 'amount of guidance or direction' refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make,

and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. **In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling.** See, *e.g., Chiron Corp. v. Genentech Inc.*, 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1326 (Fed. Cir. 2004)...In applications directed to inventions in arts where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required." As the above discussion illustrates, the art of differentiating stem cells into lung cells was unpredictable at the time of the invention, so this art must be considered "nascent," and the amount of guidance required is relatively high.

Finally, applicants present a single working embodiment in which ES cells are cultured in suspension to yield EBs and then cultured in SAGM to yield SPC-expressing cells (see page 12 of the as-filed specification). Applicant provides no particular guidance for using any other kind of cell; the statement at page 4, lines 12-17, that the stem cell can be "any pluripotent or multipotent stem cell" is not supported by the specification or the art, which even years after the invention remains unpredictable. While a singular, narrow working embodiment cannot be a sole factor in determining enablement, its limited showing, in light of the unpredictable nature of the art and the lack of direction applicants present, provides additional weight to the lack of enablement

in consideration of the *Wands* factors as a whole. Thus, one of ordinary skill in the art would not have a reasonable expectation of success in using the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites "culturing the stem cell to give an embryoid body," which is confusing because it does not particularly point out or distinctly claim the conditions necessary to effect this change. Claim 1 also recites the limitation "conditions which cause [the EB] to differentiate into cells which express surfactant protein C," which also does not particularly point out the conditions. It is not clear that one skilled in the art could determine specific conditions based on the disclosure for each and every type of stem cell. See *In re Mattison*, 509 F.2d 563, 184 USPQ 484 (CCPA 1975). Clarification is required.

Because claims 2-6 depend from indefinite claim 1 and do not clarify these points of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph.

Claim 2 is confusing because it is not clear whether the initial growth in suspension culture is part of the way in which the stem cells yield an embryoid body. Clarification is required.

Claims 3-5 do not require that the cells be physically contacted with differentiation factors, EGF, or SAGM, respectively. The nature of the interaction is not clear. Clarification is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-3 and 6 are rejected under 35 U.S.C. 102(e) as being anticipated by Mollard et al. (2005, U.S. Patent Application Publication 2005/0239201 A1; reference A). The claims are interpreted as being drawn to a method in which a stem cell is cultured under conditions that promote the formation of embryoid bodies and in which embryoid bodies are cultured under conditions that promote their differentiation to SPC-expressing cells. In some dependent claims, the stem cells are grown in suspension culture. In some dependent claims, the embryoid bodies are contacted with differentiation factors. In some dependent claims, the stem cells are ES cells.

Mollard teaches a method that comprises culturing ES cells under conditions in which they form embryoid bodies (EBs) and then culturing the EBs in a medium

comprising differentiation factors including HGF (paragraph 93). The method of Mollard yields cells that express SPC (paragraph 98). Mollard teaches that the conditions under which ES cells form EBs include suspension culture (paragraph 46).

Claims 1-6 are rejected under 35 U.S.C. 102(a) as being anticipated by Ali et al. (2002, *Tissue Engineering* 8: 541-550; reference AC on IDS). The claims are interpreted as being drawn to a method as discussed above. In some dependent claims, the differentiation conditions include EGF or SAGM, which is defined at page 12, lines 29-33, of the as-filed specification).

Ali teaches a method that comprises culturing ES cells in suspension (*i.e.*, on nonadherent culture dishes) to yield EBs, then culturing the EBs in SAGM, which comprises differentiation factors including EGF (page 542, last paragraph under "Cell culture" continued to page 543). The method of Ali yields cells that express SPC (Figure 2a, lanes 3 and 4; and page 545, first two paragraphs under "SPC mRNA expression").

Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Shannon et al. (1999, *Development* 126: 1675-1688; reference AG on IDS). The claims are interpreted as being drawn to a method as described above.

Shannon teaches a method that comprises dissociating epithelial rudiments (which comprise stem cells) and culturing them under conditions in which they form a cyst (see Figure 1B and page 1676, column 1, under "Isolation and culture...") Shannon teaches culturing the cysts in a medium comprising differentiation factors including EGF (page 1676, column 2, under "Culture medium"; and page 1677, column 2). The method of Shannon results in cells that express a distal lung epithelial cell phenotype (page

1678), including the expression by some of the cells of SPC (page 1679, column 1, paragraph 2; and Figure 5). The cysts of Shannon are "embryoid bodies" in that they are spheroid in shape and can differentiate into numerous different tissue types, including trachea and lung.

No claims are allowed. No claims are free of the art.

Applicant is requested to specifically point out the support for any amendments made to the disclosure in response to this Office action, including the claims (MPEP 714.02 and 2163.06). In doing so, applicant is requested to refer to pages and line numbers in the as-filed specification, **not** the published application. Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending U.S. applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to this Office action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lora E. Barnhart whose telephone number is 571-272-1928. The examiner can normally be reached on Monday-Thursday, 9:00am - 5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Lora E Barnhart